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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Shuwei Yang

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EXAMINER

HUTSON, RICHARD G

ART UNIT

PAPER NUMBER

1652

MAIL DATE

DELIVERY MODE

04/14/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/677,574	Applicant(s) YANG ET AL.	
	Examiner Richard G. Hutson	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2,6-9,14,17,20,37-40,69 and 75 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2,6-9,14,17,20,37-40,69 and 75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/13/2009 has been entered.

Applicant's amendment of claims 2 and 20 and the cancellation of claims 71-74, in the paper of 2/13/2009, is acknowledged.

Claims 2, 6-9, 14, 17, 20, 37-40, 69 and 75 remain present and at issue for examination.

Applicants' arguments filed on 2/13/2009, have been fully considered.

Claim Objections

Claim 20 is objected to because of the following informalities:

Claim 20 is identical to claim 2 from which it depends.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

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which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 6-9, 14, 17, 20, 37-40, 69 and 71-75 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 2, 6-9, 14, 17, 20, 37-40, 69 and 71-75. In response to this rejection applicants have amended claims 2 and 20 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection based upon a lack of written description and the rejection based upon a lack of enablement together. Applicants continue to submit that the present claims relate to Pol I type *Thermatoga neapolitana* DNA polymerases having reduced or no misincorporation of nucleotides during nucleic acid synthesis with a modification in the O-helix region defined by SEQ ID NO. 1. Applicants submit that they have amended the claims to change the transitional phrase used from “comprising” to “consisting essentially of” and that this amendment thus overcomes the rejection on the basis that as set forth in the MPEP, “consisting essentially of” limits the scope of the claim to the specified material and not to those that do not materially affect the basic and novel characteristics of the claimed invention.

Applicants submit that the rejection should be withdrawn on this basis.

Applicant's amendment and complete argument is acknowledged and has been carefully considered, however, is found nonpersuasive on the following basis.

While it is noted that applicants have changed the terminology "comprising a modification" to "consisting of a modification", it remains that the breadth of applicants claims is such that applicants do not define or describe the structure of the claimed DNA polymerase mutant beyond "the modification in the O-helix defined by SEQ ID NO: 1". It is this modification of the O-helix that applicants referred to language is directed. Given this it remains that applicants have not described the claimed mutant (i.e. the whole of the mutant) sufficiently.

Thus the previous rejection remains for the reasons made of record and repeated herein. It remains that there is no disclosure of any particular structure to function/activity relationship in the disclosed species, sufficient to describe additional mutations that reduce or eliminate misincorporation of nucleotides. The specification fails to describe additional representative species of these mutant polymerases by any identifying structural characteristics or properties other than the activities recited in claim 3, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

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Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 2, 6-9, 14, 17, 20, 37-40, 69 and 75 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Pol I type mutant The DNA polymerase wherein said The DNA polymerase consists of the specific amino acid modification of positions Arg 722 and Lys 726, does not reasonably provide enablement for any Pol I type mutant The DNA polymerase with a modification that reduces or eliminates misincorporation of nucleotides consisting essentially of: positions Arg 722 and/or Lys 726. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 2, 6-9, 14, 17, 20, 37-40, 69 and 71-75. In response to this rejection applicants have amended claims 2 and 20 and traverse the rejection as it applies to the newly amended claims.

As discussed above, applicants traverse this rejection together with the rejection based upon a lack of written description on the basis that the use of the terminology "comprising a modification" has been amended to "consisting essentially of". Applicants further submit that present claim 2 has also been amended to "omit recitation of an Arg 722 and Phe 730 double mutant" although the basis of this amendment is unclear.

Applicant's amendment and complete argument continues to be acknowledged and has been carefully considered, however, is found nonpersuasive for the reasons previously stated and repeated herein.

While it is noted that applicants have changed the terminology "comprising a modification" to "consisting of a modification", it remains that the breadth of applicants claims is such that applicants do not define or enable the extreme breadth of the genus of the claimed DNA polymerase mutant beyond "the modification in the O-helix defined by SEQ ID NO: 1". It is this modification of the O-helix that applicants referred to language is directed. Given this it remains that applicants have not enabled the claimed mutant (i.e. the whole of the mutant) sufficiently.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any Pol I type mutant Tne DNA polymerase having a modification that reduces or eliminates misincorporation of nucleotides comprising positions Arg 722 and/or Lys 726 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting polymerase, exonuclease and proofreading activity; (B) the general tolerance of Tne DNA polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a Tne DNA polymerase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain

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the polymerase, exonuclease and proofreading activity desired and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those mutant DNA polymerases of the claimed genus having the reduced or eliminated misincorporation activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any Pol I type mutant Tne DNA polymerase comprising a modification that reduces or eliminates misincorporation of nucleotides comprising positions Arg 722 and/or Lys 726. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those mutants having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,

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except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2, 6-9, 14, 17, 20, 37-40, 69 and 75 are rejected under 35 U.S.C. 102(e) as being anticipated by Chatterjee (U.S. Patent No. 5,948,614, September 1999, See IDS submitted 12/17/2003, Ref ACS).

It is noted that a similar rejection was stated in the office action sent to applicants on 4/8/2005. It is noted that the rejection was dropped based upon applicant's amendment of the claims to require that the claimed mutant be a double mutant. It is noted that applicants have removed this requirement in the amendment of the claims filed on 2/13/2009, with the amendment of "and amino acid position Lys 726..." to "and/or amino acid position Lys 726...".

Chatterjee teach a *Thermotoga* (Tne and Tma) DNA polymerases and mutants thereof. Chatterjee specifically teach a *Thermotoga* DNA polymerase mutant in which Arg 722 is substituted with Asp, Glu, Ala, Asn, Lys and His. Chatterjee also teach a mutant Tne DNA polymerase in which Lys 726 is substituted with Tyr, Arg, His and Asp thus anticipating the claims. While Chatterjee does not specifically teach that the taught modifications reduce or eliminate misincorporation of nucleotides, these are considered to be characteristics inherent to the taught DNA polymerase mutants.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rg
4/10/2009

/Richard G Hutson/
Primary Examiner, Art Unit 1652